

Immune System Dysregulation and Herpesvirus Reactivation Persist during Long-Duration Spaceflight

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BACKGROUND

Immune system dysregulation occurs during spaceflight. It is currently unknown if this phenomenon persists during long duration flight. This may represent a clinical risk to crewmembers for exploration-class missions.

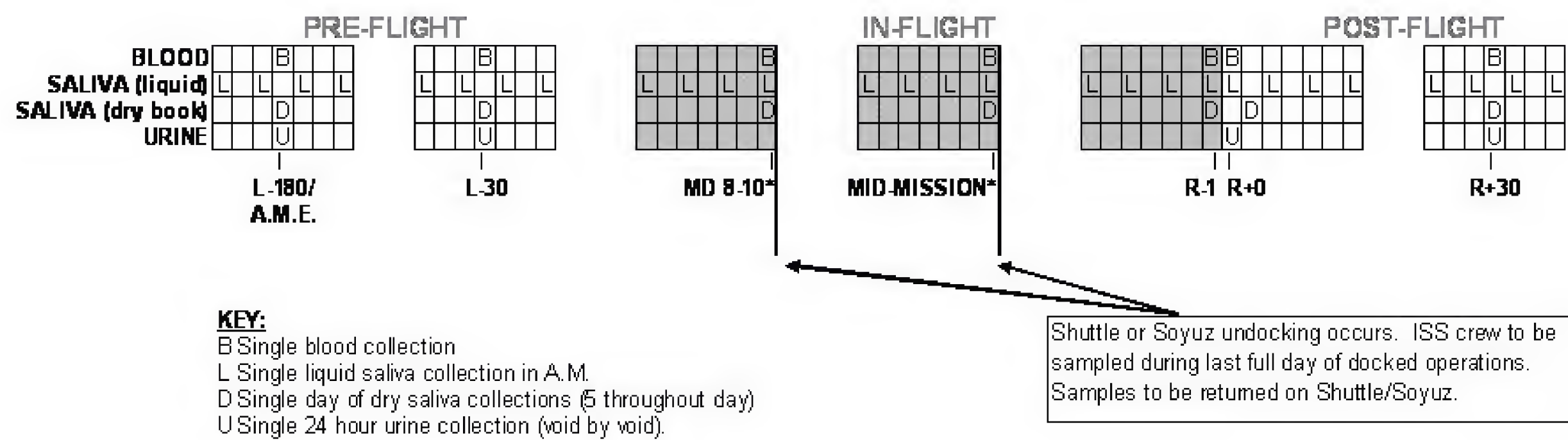
The current evidence base regarding spaceflight and immunity may be found in the NASA Human Research Program Evidence Book: http://humanresearch.isc.nasa.gov/elements/smo/hrp_evidence_book.asp. This phenomenon was also recently reviewed by Gueguinou et al: [J Leukoc Biol. 2009 Nov;86\(5\):1027-38](#).

This study, *Integrated Immune* (SMO-015), will address the following objectives:

- Determine the status of adaptive immunity, physiological stress, viral immunity, latent herpesvirus reactivation, in Astronauts during 6-month ISS missions
- Determine the clinical risk related to immune dysregulation for exploration class spaceflight.
- Determine an appropriate monitoring strategy for spaceflight-associated immune dysfunction, that could be used for the evaluation of countermeasures
- The anticipated 'n' for this study will be 17 subjects. *For this presentation, mid-point study data are presented (n = 10).*

METHODS

Blood and saliva samples were collected early, mid and late in-flight and returned for immediate analysis according to the following schedule. Functional assays were performed on ACD anticoagulated blood, which maintained viability for 48-72 hours until analysis. Specific mission dates could vary somewhat, as samples were required to be collected near a vehicle undocking for immediate sample return.



Specific assays were as follows:

- Leukocyte subsets
- T cell function
- Intracellular/secreted cytokine profiles
- Plasma cytokine balance
- Leukocyte cytokine RNA
- Virus specific T cell number
- Virus specific T cell function
- Plasma stress hormones
- Latent herpesvirus reactivation (saliva/urine)
- Saliva/urine stress hormones
- Circadian rhythm analysis

All methods used for this study were performed as previously described: *Aviation and Space Environmental Medicine, 2009 May, 80(5 Suppl): A37-44*.



Integrated Immune blood collection onboard the International Space Station



Integrated Immune on-orbit blood collection kit (top) and liquid/dry saliva collection kit (right)

Table 1: Mean general immune data, ISS, n=10 (red = consistent mission trend; * = statistically significant; p<0.05)

PERIPHERAL LEUKOCYTE SUBSETS

	L-180	L-45	Early	Mid	Late	R+0	R+30
WBC	4.6	4.9	5.4	4.9	4.9	7.6	4.7
Granulocytes	59	56	61	62	62	74*	59
Lymphocytes	33	36	32	32	30	19*	33
Monocytes	5.9	7.0	4.5	4.5*	3.9*	4.9*	7.1
T Cells	72	72	72	73	70	68	71
B Cells	8	9	14*	10	12*	14*	9
NK Cells	8	6	6	9	10	9	9
CD4+ T Cells	62	63	63	62	64	61	63
CD8+ T Cells	33	32	30	32	31	32	32
Bulk Memory CD4+	60	61	62	64	64	66*	60
Bulk Memory CD8+	43	43	46*	47	46	46	44
Non Differentiated	47	46	43	46	44	42	42
Active Cytotoxic	25	26	32	40*	38	40*	37
Stresscoat	24	23	19	10*	15	15	20
Treg	26	33	26	26	28	29	30
Central memory	20	19	24	17	21	19	20
Effector Memory	35	32	39	39	39	34	34
Term Differentiated	17	16	13	19	17	19	20
CD4/CD8	1	1	6	3	2	2	3
CD8/CD8	2	2	6	4	5	4	3
CD4/HLA-DR	3	2	2	2	1	2	2
CD8/HLA-DR	7	4	4	3	3	3	4

INTRACELLULAR CYTOKINE PROFILES

	L-180	L-45	Early	Mid	Late	R+0	R+30
CD4/IL-2	48	47	39	48	49	36*	49
CD8/IFN γ	26	34	27	32	29	33	29
SEA+SEA 24hr	L-180 <td>L-45<td>Early<td>Mid<td>Late<td>R+0<td>R+30</td></td></td></td></td></td>	L-45 <td>Early<td>Mid<td>Late<td>R+0<td>R+30</td></td></td></td></td>	Early <td>Mid<td>Late<td>R+0<td>R+30</td></td></td></td>	Mid <td>Late<td>R+0<td>R+30</td></td></td>	Late <td>R+0<td>R+30</td></td>	R+0 <td>R+30</td>	R+30
CD4/IFN γ	44	45	26*	36	34	44	45
CD8/IFN γ	42	43	29*	32	35	49	43
CD4/IL-2/5	27	28	10*	17*	17*	29	29
CD8/IL-2/5	19	21	10*	13*	15	26	18
SEA 24hr	L-180 <td>L-45<td>Early<td>Mid<td>Late<td>R+0<td>R+30</td></td></td></td></td></td>	L-45 <td>Early<td>Mid<td>Late<td>R+0<td>R+30</td></td></td></td></td>	Early <td>Mid<td>Late<td>R+0<td>R+30</td></td></td></td>	Mid <td>Late<td>R+0<td>R+30</td></td></td>	Late <td>R+0<td>R+30</td></td>	R+0 <td>R+30</td>	R+30
CD4/IFN γ	54	49	50	52	49	53	44
CD8/IFN γ	60	57	59	60	57	56	53
CD4/IL-2/5	39	37	27	32	30	36	32
CD8/IL-2/5	34	35	25	27	29	29	33
CD4/IFN γ	17	22	1*	2*	4*	12	19
CD4/IL-2	17	22	1*	2*	4*	12	19
CD4/IL-5	17	22	1*	2*	4*	12	19
CD4/IL-6	17	22	1*	2*	4*	12	19
CD4/IL-10	17	22	1*	2*	4*	12	19
CD4/IL-17	17	22	1*	2*	4*	12	19
CD4/IL-18	17	22	1*	2*	4*	12	19
CD4/IL-19	17	22	1*	2*	4*	12	19
CD4/IL-20	17	22	1*	2*	4*	12	19
CD4/IL-21	17	22	1*	2*	4*	12	19
CD4/IL-22	17	22	1*	2*	4*	12	19
CD4/IL-23	17	22	1*	2*	4*	12	19
CD4/IL-24	17	22	1*	2*	4*	12	19
CD4/IL-25	17	22	1*	2*	4*	12	19
CD4/IL-26	17	22	1*	2*	4*	12	19
CD4/IL-27	17	22	1*	2*	4*	12	19
CD4/IL-28	17	22	1*	2*	4*	12	19
CD4/IL-29	17	22	1*	2*	4*	12	19
CD4/IL-30	17	22	1*	2*	4*	12	19
CD4/IL-31	17	22	1*	2*	4*	12	19
CD4/IL-32	17	22	1*	2*	4*	12	19
CD4/IL-33	17	22	1*	2*	4*	12	19
CD4/IL-34	17	22	1*	2*	4*	12	19
CD4/IL-35	17	22	1*	2*	4*	12	19
CD4/IL-36	17	22	1*	2*	4*	12	19
CD4/IL-37	17	22	1*	2*	4*	12	19
CD4/IL-38	17	22	1*	2*	4*	12	19
CD4/IL-39	17	22	1*	2*	4*	12	19
CD4/IL-40	17	22	1*	2*	4*	12	19
CD4/IL-41	17	22	1*	2*	4*	12	19
CD4/IL-42	17	22	1*	2*	4*	12	19
CD4/IL-43	17	22	1*	2*	4*	12	19
CD4/IL-44	17	22	1*	2*	4*	12	19
CD4/IL-45	17	22	1*	2*	4*	12	19
CD4/IL-46	17	22	1*	2*	4*	12	19
CD4/IL-47	17	22	1*	2*	4*	12	19
CD4/IL-48	17	22	1*	2*	4*	12	19
CD4/IL-49	17	22	1*	2*	4*	12	19
CD4/IL-50	17	22	1*	2*	4*	12	19
CD4/IL-51	17	22	1*	2*	4*	12	19
CD4/IL-52	17	22	1*	2*	4*	12	19
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CD4/IL-60	17	22	1*	2*	4*	12	19
CD4/IL-61	17	22	1*	2*	4*	12	19
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CD4/IL-64	17	22	1*	2*	4*	12	19
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CD4/IL-67	17	22	1*	2*	4*	12	19
CD4/IL-68	17	22	1*	2*	4*	12	19
CD4/IL-69	17	22	1*	2*	4*	12	19
CD4/IL-70	17	22	1*	2*	4*	12	19
CD4/IL-71	17	22	1*	2*	4*	12	19
CD4/IL-72	17	22	1*	2*	4*	12	19
CD4/IL-73	17	22	1*	2*	4*	12	19
CD4/IL-74	17	22	1*	2*	4*	12	19
CD4/IL-75	17	22	1*	2*	4*	12	19
CD4/IL-76	17	22	1*	2*	4*	12	19
CD4/IL-77	17	22	1*	2*	4*	12	19
CD4/IL-78	17	22	1*	2*	4*	12	19
CD4/IL-79	17	22	1*	2*	4*	12	19
CD4/IL-80	17	22	1*	2*	4*	12	19
CD4/IL-81	17	22	1*	2*	4*	12	19
CD4/IL-82	17	22	1*	2*	4*	12	19
CD4/IL-83	17	22	1*	2*	4*	12	19
CD4/IL-84	17	22	1*	2*	4*	12	19
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CD4/IL-87	17	22	1*	2*	4*	12	19
CD4/IL-88	17	22	1*	2*	4*	12	19
CD4/IL-89	17	22	1*	2*	4*	12	19
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CD4/IL-91	17	22	1*	2*	4*	12	19
CD4/IL-92	17	22	1*	2*	4*	12	19
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CD4/IL-94	17	22	1*	2*	4*	12	19
CD4/IL-95	17	22	1*	2*	4*	12	19
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CD4/IL-97	17	22	1*	2*	4*	12	19
CD4/IL-98	17	22	1*	2*	4*	12	19
CD4/IL-99	17	22	1*	2*	4*	12	19
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CD4/IL-103	17	22	1*	2*	4*	12	19
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CD4/IL-125	17	22	1*	2*	4*	12	19
CD4/IL-126	17	22	1*	2*	4*	12	19
CD4/IL-127	17	22	1*	2*	4*	12	19
CD4/IL-128	17	22	1*	2*	4*	12	19
CD4/IL-129	17	22	1*	2*	4*	12	19
CD4/IL-130	17	22	1*	2*	4*	12	19
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CD4/IL-133	17	22	1*	2*	4*	12	19
CD4/IL-134	17	22	1*	2*	4*	12	19
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CD4/IL-171	17	22	1*	2*	4*	12	19
CD4/IL-172	17	22	1*	2*	4*	12	19
CD4/IL-173	17	22	1*	2*</			